

Regional cortical thinning is associated with cognitive status in Parkinson’s disease

Mustafa M Almuqbel^{1,2}, Tracy R Melzer^{1,2,3}, Daniel J Myall², Michael R MacAskill^{1,2}, Leslie Livingston^{1,2}, Kyla-Louise Horne^{2,4}, Toni L Pitcher^{1,2}, Ross J Keenan^{2,5}, John C Dalrymple-Alford^{1,2,3,4} and Tim J Anderson^{1,2,3,6}

¹Department of Medicine, University of Otago, Christchurch, New Zealand; ²New Zealand Brain Research Institute, Christchurch, New Zealand; ³Brain Research NZ (Rangahau Roro Aotearoa), New Zealand; ⁴Department of Psychology, University of Canterbury, New Zealand; ⁵Christchurch Radiology Group, Christchurch, New Zealand; ⁶Department of Neurology, Christchurch Hospital, Christchurch, New Zealand.

1 Parkinson’s disease (PD) at a glance

PD: A neurodegenerative movement disease.
Prevalence: Affects up to 2% of individuals over 60.
Risk factors: Age.
Diagnosis: Clinical & neuropsychological assessment
Symptoms: Motor: tremor, slow movement, rigidity;
Cognitive: impairments in multiple domains, including attention, executive, function, and memory;
Others: sleep disturbance and swallowing difficulties.
Treatment: Medications & Surgical (motor symptoms only).

2 The challenge

As the disease progresses, cognitive impairments become more manifest in many patients, ultimately leading to dementia in the majority. However, there is considerable variation (range 2-20 years) between onset of the initial motor disorder and the emergence of dementia.¹ Importantly, this delay provides a window for potential therapeutic intervention.
Detecting cognitive impairment at its earliest stages would facilitate the most appropriate and timely intervention aimed at slowing the progression to dementia.
However, the assessment of neuroprotective and disease-modifying therapies in PD has been hampered by a lack of clinically useful, reliable neurobiomarkers.

3 The proposed solution

Cortical thickness derived from structural magnetic resonance imaging (MRI) T1-weighted images provides a potential marker of cognitive decline in PD.²

4 Aim

To investigate whether cortical thickness is associated with cognitive impairment in Parkinson’s disease.

5 Methods

- 168 subjects (117 PD and 51 controls) were included in this study.
- All subjects completed a neuropsychological battery and were classified as healthy controls (**HC**), PD with normal cognition (**PDN**), PD with mild cognitive impairment (**PDMCI**, MDS level-II), or PD with dementia (**PDD**) (**Table 1**).
- All subjects underwent MRI examination.
- Three-dimensional T1-weighted (spoiled gradient echo acquisition, TE/TR=2.8/6.6ms, TI=400ms, voxel size=0.98×0.98×1.0mm³) images were acquired on a 3T GE HDxt scanner (**Figure 1, A**).
- The Freesurfer was used to quantify cortical thickness (**Figure 1, B**).
- We used a general linear model with age, sex and unified Parkinson's disease rating scale (UPDRS-III) as covariates to assess cortical thickness across cognitive subgroups.

6 Results

Cortical thickness (all groups), figure 2:

- PDN < HC**, PDN had significant cortical thinning in the left parietal and frontal lobes.
- PDMCI < HC**, PDMCI had significant cortical thinning bilaterally in the temporal and parietal lobes; and in the left frontal and occipital regions.
- PDD < HC**, PDD had significant bilateral cortical thinning in the temporal, frontal parietal, cingulate, occipital and insular areas.

Cortical thickness (PD sub-groups), figure 3:

- PDD < PDMCI**, PDD had significant cortical thinning in the left frontal and parietal regions.
- PDMCI < PDN**, PDMCI had significant cortical thinning bilaterally in the temporal lobes cortices and the left parietofrontal region.
- PDD < PDN**, PDD had significant cortical thinning bilaterally in the temporal, frontal and parietal areas.

Association, figure 4:

- Cortical thinning was significantly associated with subjects’ cognitive decline (cognitive Z score) bilaterally in the parietal, frontal and temporal regions.

7 Conclusion

- In this large group of PD patients we conclude that cortical thickness measured by MRI may be a potential marker for cognitive impairment in PD.
- Additional work is underway to determine whether the longitudinal rate of change of cortical thickness is predictive of conversion to dementia in PD patients.

References:

¹ Litvan I, et al. Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Movement disorders 2012;27:349-356.
² Pereira J B, et al. Initial cognitive decline is associated with cortical thinning in early Parkinson disease. Neurology. vol. 82, pp. 2017-2025, 2014.

Acknowledgements: The authors gratefully acknowledge support funding from the Neurological Foundation of New Zealand, the Neurology Trust, Canterbury Medical Research Foundation, the Saudi Arabian Government Scholarship Program and the Health Research Council of New Zealand.

Table 1. Demographic and neuropsychological data by group

	Controls (HC)	PDN	PDMCI	PDD
n	51	68	29	20
Sex (M/F)	34/17	44/24	20/9	19/1
Age (years)	69(8)	64(9)*	70(7)	74(7)*
Education (years)	13(3)	13(3)	13(3)	13(2)
Cognitive Z score	0.60(0.4)	0.24(0.4)*	-0.8(0.3)*	-1.7 (0.5)*
MoCA	27.0(2.1)	26.4(2.3)	22.7(2.3)*	16.9(4.0)*
Disease duration(years)	NA	2.2(3)	4.7(6) ^Δ	11(8) ^Δ
LED (mg/day)	NA	204(298)	302(399) ^Δ	717(390) ^Δ

Values are mean (sd). *p<0.001 significant ANOVA with post-hoc difference between control and PD subgroups & ^Δp<0.001 between PDN and the other PD groups. LED = levodopa equivalent dose. MoCA = Montreal cognitive assessment. Cognitive Z score = global cognitive ability derived from the neuropsychological battery.

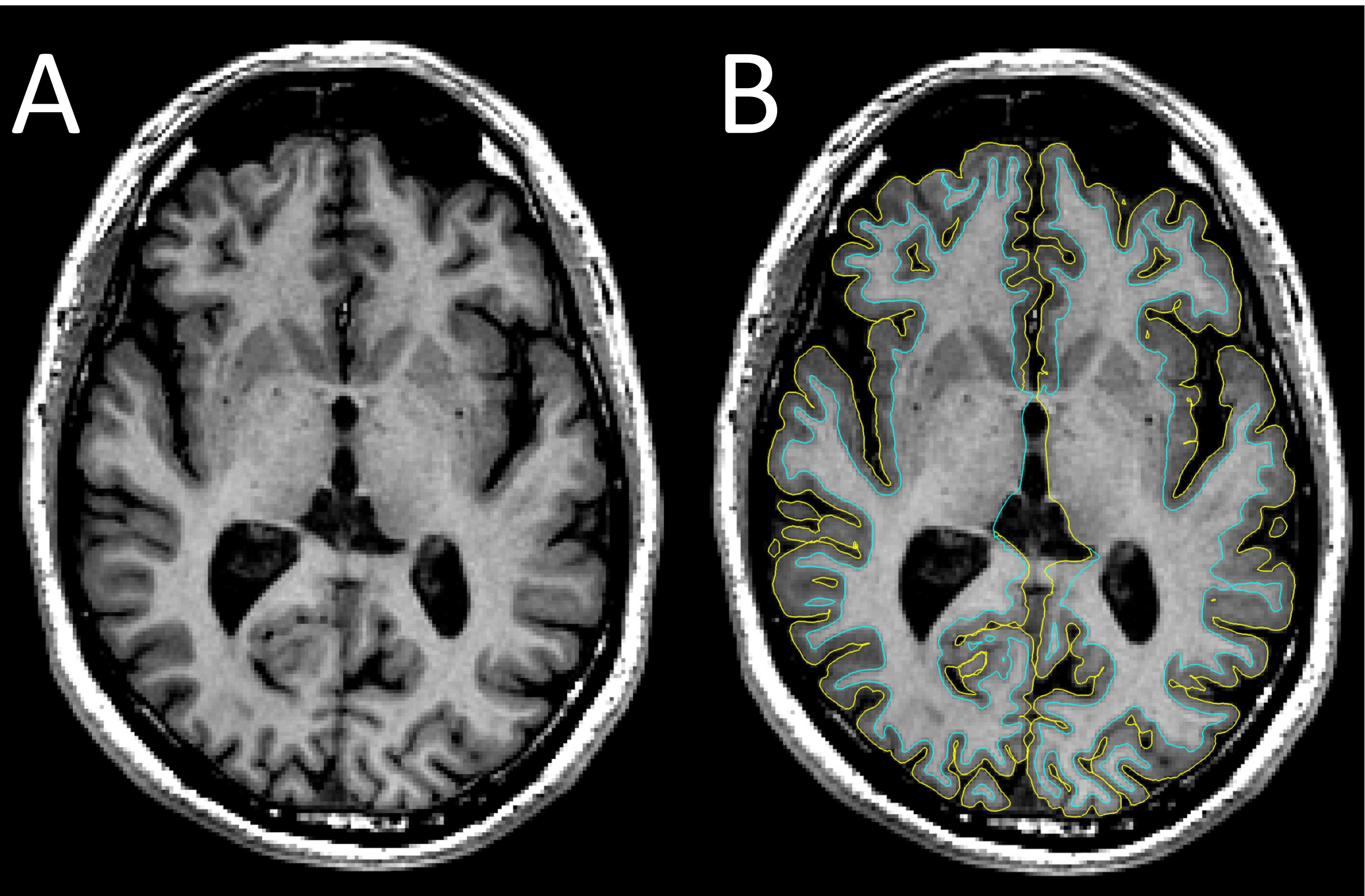


Figure 1. (A) Axial T1-wieghted image of the brain and (B) the same image with Freesurfer software delineating the cortex.

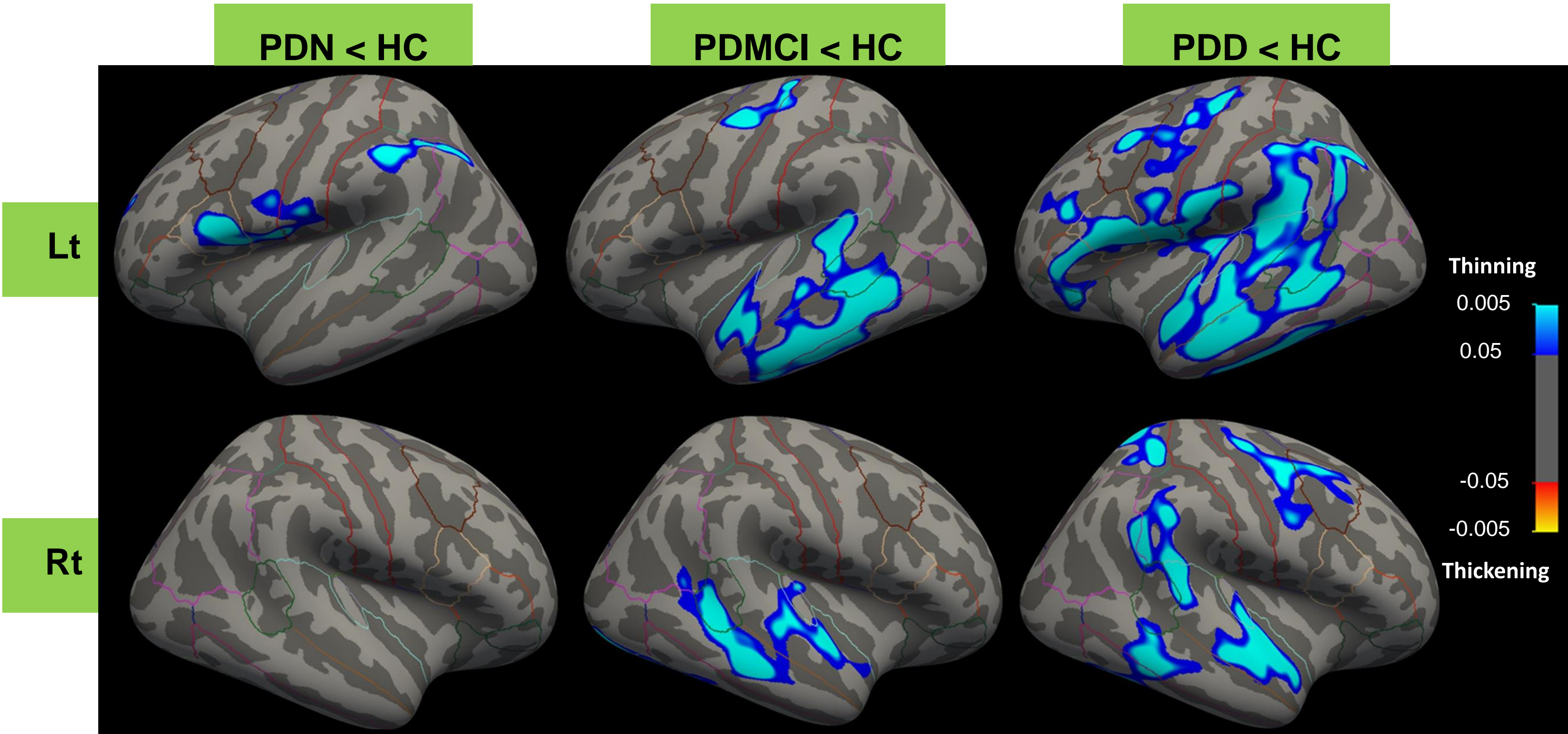


Figure 2. Vertex-wise cortical thinning significance maps of PDN, PDMCI and PDD relative to controls. Cluster-wise correction for multiple comparisons (Monte-Carlo Simulation, p<0.05).

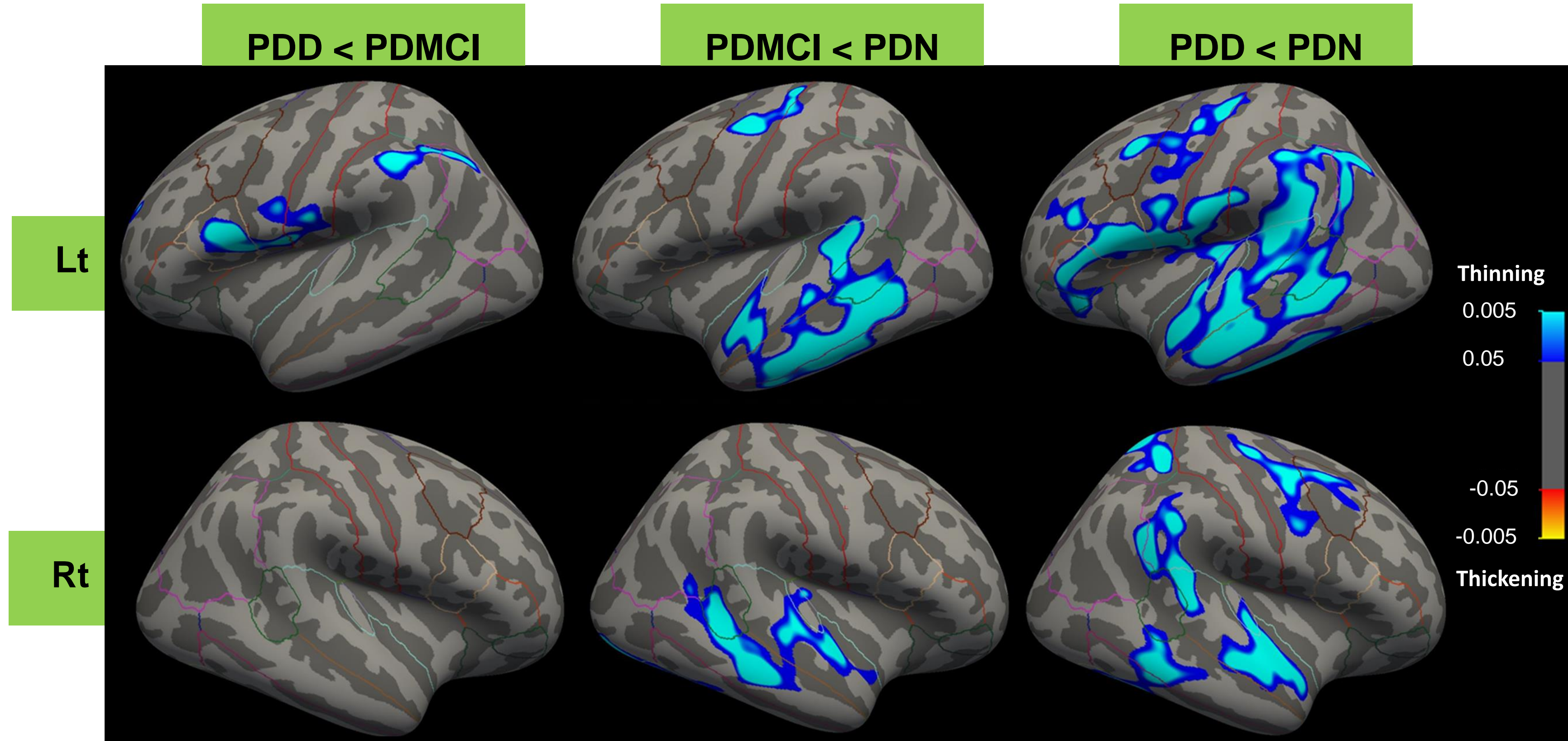


Figure 3. Vertex-wise cortical thinning significance maps of PDMCI and PDD relative to PDN; and PDD relative to PDMCI. Cluster-wise correction for multiple comparisons (Monte-Carlo Simulation, p<0.05).

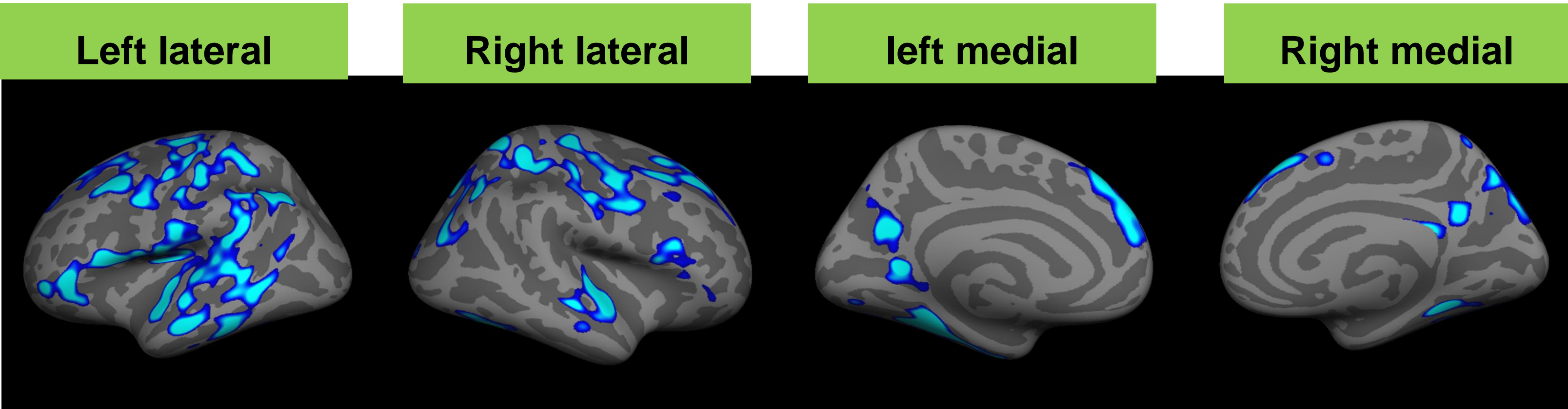


Figure 4. Vertex-wise significance maps of the correlation between cortical thinning and subjects’ cognitive decline (Z score) . Cluster-wise correction for multiple comparisons (Monte-Carlo Simulation, p<0.05).